Evaluation of Relationships Between Mainstream Smoke Acetaldehyde *and* "Tar" and Carbon Monoxide Yields in Tobacco Smoke and Reducing Sugars in Tobacco Blends of U.S. Commercial Cigarettes

by

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SUMMARY

Mainstream smoke acetaldehyde, carbon monoxide and "tar" yields and percentage total reducing sugars in the tobacco blends from a Philip Morris database of a large number of commercial US cigarettes was analyzed. MS smoke acetaldehyde is significantly correlated with "tar" yield and also with MS smoke carbon monoxide. The correlations found between MS smoke acetaldehyde yield *and* "tar" and MS smoke carbon monoxide support the conclusion that both acetaldehyde and carbon monoxide yields are affected more by cigarette design characteristics influencing total smoke production, such as filter ventilation, than by specific tobacco additives. MS smoke acetaldehyde yield is not correlated with reducing sugar concentration in the tobacco blend. For the available data over the time periods 1985-1993, the concentration of reducing sugars (mean values for the brands tested) decreased. The correlations and conclusions reported herein are consistent with the published literature, including the 1999 Massachusetts Benchmark Study.

INTRODUCTION

Acetaldehyde (**1**; referred to as "AA" herein) has recently been classified as being a smoke constituent with significant potential biological activity.[1,2] The US Consumer Products Safety Committee identified acetaldehyde as a cigarette smoke constituent of concern,[3] and a study by the World Health Organization indicated that AA may be cytotoxic or genotoxic.[2] Two recent reports suggested that MS smoke acetaldehyde is derived from sugars added in tobacco processing.[4,5] A recent review of the scientific

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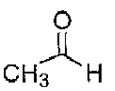
literature concluded that MS smoke acetaldehyde yields are affected more by cigarette design characteristics influencing total smoke production, such as filter ventilation, than by specific additives such as sugars, e.g., D-glucose (**2**, illustrated in its β-glucopyranose form **2-βgp**; see Figure 1).[6] This review further concluded that natural tobacco polysaccharides, e.g., cellulose (**3**), are likely to be the primary precursors of mainstream (MS) smoke acetaldehyde (**1**). In order to focus the development of potentially reduced-harm tobacco products and to address real scientific and technical issues, it is critical to identify accurately the source(s) of MS smoke acetaldehyde.



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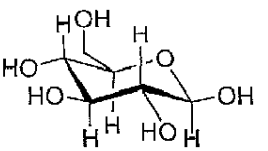

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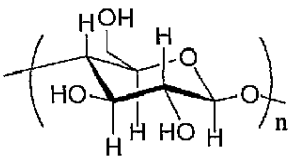

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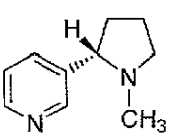
The purpose of this study is to analyze the available data on commercial cigarettes over a period of many years, which includes data on tobacco blend reducing sugars (RS), MS smoke acetaldehyde yields and MS smoke carbon monoxide yields. We shall examine the hypothesis that sugars in tobacco lead to MS smoke acetaldehyde. We shall also examine if reducing sugar levels in tobacco blends of commercial cigarettes have increased for the years that complete and statistically meaningful data is available. By "complete and statistically meaningful data", we mean having a large enough data set of commercial cigarettes for which measurements were made of the tobacco and/or smoke parameters of interest.

MS smoke nicotine (**4**) and "tar" yields have been measured and reported for US commercial cigarettes over the past decades. Measurement of MS smoke acetaldehyde yields for a series of commercial cigarettes have been reported only sporadically.[6-9] There are two types of sugars in the tobacco blend: reducing sugars and non-reducing sugars. Reducing sugars are those sugars that can tautomerize and isomerize upon dissolution in water.[10] All monosaccharides are reducing sugars. For example, D-glucose (**2**) and D-fructose (**5**, see Figure 1) are both reducing sugars because they can exist as a hemiacetal or hemiketal, respectively and can isomerize to each other and to other monosaccharides via enediols (e.g., **6**) as shown in Figure 1.[11]



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Fortunately, the Philip Morris USA database contains data for both MS smoke acetaldehyde yield data and reducing sugars in the tobacco blend for a large number of

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US commercial cigarettes in the same time period. Limited data is available on carbon monoxide yields. The data originates from cigarettes sold in the United States in the years 1985-1988 and 1990-1993, including brands manufactured by corporations other than Philip Morris. All relevant data within the database was used in this work to examine the relationships between MS acetaldehyde yield *and* "tar" yields, carbon monoxide yields, and RS in tobacco.

The "1999 Massachusetts Benchmark Study" has recently become available.[7] This collaborative study of Brown & Williamson Tobacco Corporation, Lorillard Tobacco Company, Philip Morris, USA, and R. J. Reynolds Tobacco Company, is comprehensive, in terms of the range of US commercial brands studied, the number of MS and sidestream (SS) smoke constituents quantified, the variety of analytical and statistical tools utilized, and the number of scientists and laboratories involved. MS smoke data was reported for acetaldehyde using a modified Massachusetts Benchmark Study (MBS) puff profile and FTC and MBS "tar", and FTC and MBS MS smoke carbon monoxide, among other smoke constituents. (A description of the various puff profiles is given in Table 1.) In 1997, Labstat Inc. produced a study of ten commercial US cigarettes in which MS smoke nicotine, "tar", and acetaldehyde smoke yields were reported.[8] And most recently, Chepiga, et al. reported relevant smoke constituent yields for a set of 26 US commercial cigarettes.[9]

We herein report an evaluation of this data and observe (1) that MS smoke acetaldehyde is highly correlated with "tar" and, when measured, with MS smoke carbon monoxide for these different sets of US commercial cigarettes; (2) neither MS smoke AA nor the ratio AA/"tar" is correlated with reducing sugars in the tobacco blend; and (3) for the available data over the time periods 1985-1993, the concentration of reducing sugars (mean values for the brands tested) decreased. These results for a wide range of US commercial cigarettes indicate that MS smoke acetaldehyde yields are affected more by cigarette design characteristics influencing total smoke production, such as filter ventilation, than by specific additives such as reducing sugars.

EXPERIMENTAL

Nicotine and "tar" yields were determined using the standard FTC protocol.[12-15] For cigarettes manufactured prior to 1990, MS smoke carbon monoxide and acetaldehyde (as total aldehydes) were determined as follows. Because acetaldehyde is by far the major gas phase aldehyde in MS smoke, total gas phase aldehydes was used for many years as a surrogate for MS smoke acetaldehyde[6,16-18] Gas phase was analyzed using a 5-port smoking machine with a manifold system. The smoke was split by a series of gas sampling valves, and aliquots of gas phase smoke were delivered to the respective detectors. Carbon monoxide was analyzed on a nondispersive infrared (NDIR) spectrophotometer. A second aliquot was forced by positive air pressure through a deionized water scrubbing tower for the entrapment of total aldehydes prior to their colorimetric determination by a continuous flow procedure. The water-soluble aldehydes

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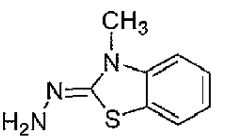
form a colored species when condensed with 3-methyl-2-benzothiazolinone hydrazine (7) in the presence of an oxidizing agent ($FeCl_3$-HNO_3). The results are expressed as total acetaldehydes when compared to aqueous formaldehyde standards. For cigarettes manufactured in 1990 and analyzed for MS smoke aldehydes (116 brands), 112 were analyzed using the method described above. The other four brands manufactured in 1990 and all cigarettes manufactured subsequent to 1990 were analyzed in the following manner. A 5-port smoking machine was configured with a Fourier Transform Infrared (FTIR) analyzer that analyzed carbon monoxide and acetaldehyde in cigarette smoke directly after exiting the smoking manifold. To assess precision accuracy and precision of the tobacco and smoke parameters measured herein, either an Industry Monitor (for "tar") or a standard gas sample (for CO and acetaldehyde) was used routinely during the analyses.



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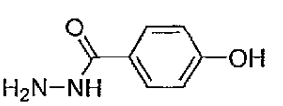
Reducing sugars were extracted from cigarette filler with an aqueous acetic acid solution and determined colorimetrically using a continuous flow procedure. Reducing sugars were determined by their reaction with 4-hydroxybenzoic acid hydrazide (**8**) in a basic medium to form a color thought to be a phenylosazone, e.g., **9** (Figure 2).[10,19-21] Instrument calibration standard was a 1:1 D-glucose:D-fructose mixture. To validate instrument performance, several "monitor" samples were prepared and analyzed on the instrument along with the unknown samples. This monitor (or secondary reference material) was generally a large batch of cigarette filler tobacco that was ground in a Wiley mill, mixed thoroughly, placed into jars, sealed, and kept in cold storage. The monitor was extensively tested to determine mean, SD, and control limits. Jars of the monitor were opened and used as needed on instrument runs. The results of the monitor were compared to the established control limits and that data was used as part of the process to validate an instrument run.



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METHODS OF COMPARING SMOKE YIELD DATA

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In analyses of tobacco and MS smoke data, three types of relationships can be evaluated:

Case (1): One tobacco constituent with a MS smoke constituent;
Case (2) One MS smoke constituent with a second MS smoke constituent.
(a) One smoke constituent exists primarily in the gas phase, the second in the particulate phase.
(b) Both smoke constituents exist primarily in the same phase.

Consider Case 1. The question frequently arises, "does tobacco component ABC yield mainstream smoke constituent XYZ?" The most direct experimental method to answer this question is to label ABC with, for example, ^{14}C and determine the smoke yield of ^{14}C-XYZ.[22,23] An indirect method is to compare the MS smoke yield of XYZ from two cigarettes, a control and a control to which substrate ABC had been added to the tobacco blend. This latter method suffers from a subtle complexity. If XYZ does yield ABC in MS smoke but does so in an overall yield equivalent to the average yield of XYZ from the tobacco blend itself, then substituting ABC for an equivalent weight of tobacco blend will result in the same MS yield of XYZ. Thousands of compounds are known to be present in both tobacco and tobacco smoke. Of particular interest is whether a specific tobacco component or additive forms a specific smoke constituent in a yield that *exceeds* the global yield efficiency (weight of smoke constituent per weight of tobacco burnt during puffing) from non-specific transformations from the thousands of tobacco blend components themselves. In this work, we shall interpret the phrase "tobacco component ABC yields mainstream smoke constituent XYZ" to mean that the yield efficiency exceeds that from the tobacco blend itself.

One must also demonstrate that the smoke chemistry is not altered by the presence of XYZ, e.g., the puff count and "tar" yield is not changed. When examining the relationship between a tobacco component with a MS smoke constituent, one may have to normalize the smoke constituent to total smoke formation. For example, one might ask the question, "Does the addition of reducing sugars (an example of 'XYZ') to tobacco cause an increase in MS smoke acetaldehyde?" One approach to answering this question would be to compare the MS smoke yields of acetaldehyde within a series of cigarettes containing varying levels of reducing sugars in the tobacco blend.

An important understanding must now be made. One must examine not just the variation in MS smoke acetaldehyde yield but rather the variation in MS smoke acetaldehyde yield *relative* to the yield of total smoke formation. "Total smoke formation" can be estimated by TPM, or "tar", or possibly "total gas phase yield," or even a surrogate for these parameters, e.g., nicotine yield for "tar" or carbon monoxide yield for "total gas phase yield".[7] If the levels of MS smoke acetaldehyde do vary, for example, with the same multiplier as "tar" yield or carbon monoxide yield varied, then no "selective" variation of MS smoke acetaldehyde would have been found relative to RS in the tobacco.

In other words, one must demonstrate the finding of a "specific" or "selective" variation (increase or decrease) of a constituent's MS smoke yield compared to the MS

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smoke yield of all other relevant smoke constituents. If a "global" increase or decrease is observed upon the addition of a tobacco blend component, this may reflect an increase in total smoke formation. One cause for such a global variation could be a change in burn rate characteristics, increasing or decreasing puff count, increasing or decreasing ventilation, etc.

Consider Case 2. When both parameters are MS smoke constituents, examination of a direct correlation between the MS smoke yields of the two substances is appropriate. In this case, it is not necessary to normalize one or both constituents relative to "tar".

In some instances, useful information may be obtained by considering the relationship between the ratio "MS smoke constituent XYZ"/'tar'" *and* "tar" yield. In this type of analysis, one could examine if the "tar"-normalized yield of a smoke constituent varied as the "tar" yield itself increased or decreased. If one were to examine "MS smoke constituent XYZ"/'tar'" as a function of "tar", one would have to take into consideration a deceptively simple but in fact complex situation. As "tar" decreased to very low yields, all other smoke constituent yields would also decrease substantially. The ratio "MS smoke constituent XYZ"/'tar'" might, for example, *increase* while both "MS smoke constituent XYZ" and "tar" might *substantially decrease*.

In this work, mean values of tobacco and smoke constituents were calculated directly, i.e., without any weighting for variation in sales. We chose this approach for a number of related reasons. Fundamentally, we were interested in understanding tobacco-smoke precursor product relationships and related tobacco smoke chemical and physical issues.

THE RELATIONSHIP BETWEEN MS SMOKE ACETALDEHYDE AND "TAR" *OR* MS SMOKE CARBON MONOXIDE

Acetaldehyde is a gas at room temperature and pressure; its boiling point at atmospheric pressure is 21°C. A very reactive substance, acetaldehyde likely undergoes some degradation during trapping and during analysis and possibly prior to exiting the cigarette.[23] Table 2 compares acetaldehyde with nicotine in terms of some physical and smoke chemistry properties.

The AA and "tar" data from the Philip Morris database for 1985-1988 and 1990-1993 are summarized in Table 3. The data sets for these years were selected for our analysis on the basis that simultaneous measurements of the parameters of interest were made across a wide spectrum of commercial brands, representing a large sample of cigarettes in the marketplace. In some instances in this work, the data for one set of correlations derived from a collection of cigarette brands, which was *not* identical to the cigarette brands for which data was available for another correlation. The available data for other years was limited either by restricted sampling of the marketplace or incomplete measurement of the parameters of interest.

The mean values of FTC MS smoke acetaldehyde are relatively constant from 1985 to 1993 (ca. 0.52 mg/cigarette) for the cigarettes reported in the data base (ranging from

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196-492 brands). In all years, a wide range of yields is observed. Similarly, "tar" yields appear to be somewhat constant during the 1985 to 1993 period (ca. 10.8 mg).

Table 4 lists the MS smoke acetaldehyde and "tar" yields for US commercial cigarettes reported in three recent studies. In the Labstat study, "tar" was determined using the first three puff profiles listed inTable 1 while AA was measured using only the FTC profile. In contrast, in the Massachusetts Benchmark Study, "tar" yields were measured using both the FTC and another puff profile, the MBS profile, while MS smoke acetaldehyde yield was determined using only the MBS profile. The recent Chepiga, et al. work used the FTC puff profile.

Of particular importance is the uniform observation of excellent correlations between MS smoke acetaldehyde and "tar" using the linear model (eq. 1) These are summarized in Tables 5-7.

$$\text{MS smoke acetaldehyde yield} = \text{slope} \times (\text{"tar"}) + \text{intercept} \qquad (1)$$

Table 5 lists the statistics for the relationship between MS smoke acetaldehyde delivery vs. "tar" for the brands tested in the 1985-1988 and 1990-1993 time periods using data from the Philip Morris database. Linear relationships are observed, though with a fair amount of scatter, as quantified by r^2 values from 0.79-0.87. Two representative correlations are shown in Figures 3-4 for 1985 and 1992, respectively. Throughout the time period studied, the slopes and intercepts of the lines appear to be very similar. In fact, the consistency of the values of the slopes (0.038-0.051; viz. Table 5) suggests that the correlations actually reflect a tobacco-smoke chemistry relationship between these two parameters rather than a mere statistical association. This is because MS smoke AA is fundamentally a pyrolysis/combustion product from the tobacco, as are many of the thousands of constituents in "tar".

As shown in Table 6, the Massachusetts Benchmark Study reported two second order (quadratic equations) correlations, between MS smoke acetaldehyde with "tar" (r^2 = 0.8209) as well as with MS smoke carbon monoxide (r^2 = 0.9257). No explanation was provided by the authors for the use of a second order correlation model, except for their notation that this is the form currently used by tobacco manufacturers in the United States in their report to the Commonwealth of Massachusetts which incorporates the so-called "Massachusetts nicotine multiplier".[7]

$$\text{MS smoke acetaldehyde yield} = \underline{a}\,(\text{"MS CO"})^2 + \underline{b}\,(\text{"MS CO"}) + \underline{c} \qquad (2)$$

where $\underline{a}$, $\underline{b}$, and $\underline{c}$ are constants.

In contrast, the Labstat data revealed either equivalent or superior correlations between MS smoke AA and "tar", compared with MS smoke AA and MS smoke carbon monoxide (see Table 7).[8] The Labstat study contains data for three different puff profiles for "tar", but in one (FTC), "tar" yield for only eight of the ten cigarettes studied is reported. The Chepiga, et al. study obtained a superior correlation between MS AA yield and "tar" (r^2 = 0.91) using the FTC puff profile.

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The Philip Morris database contained MS smoke acetaldehyde and carbon monoxide yields for the same cigarettes in only two years, 1985 and 1993 (116 and 117 brands for these years, respectively). A summary of the data is shown in Table 8. Carbon monoxide data is available for fewer brands than for "tar" and for MS smoke acetaldehyde, as seen by a comparison of the data in Table 3 with the data in Table 8. Excellent correlations are observed between MS smoke acetaldehyde and MS smoke carbon monoxide (Table 9), with $r^2 = 0.833$ and 0.934 for 1985 and 1993 data respectively. The correlation for 1993 is shown in Figure 5. These correlations are superior to those between MS smoke acetaldehyde and "tar" for the same years ($r^2 = 0.701$ and 0.832 for 1985 and 1993 data respectively; $n = 30$ and 135), though the cigarette brands included in the correlations are not the same. That acetaldehyde and CO correlate better than acetaldehyde and "tar" is consistent with the observations in the Massachusetts Benchmark study,[7] though not with the more limited Labstat data set,[8] and may well be related to the phase of the smoke constituent.

These four data sets represent smoke data for various sets and years of US commercial cigarettes. Taken together, the data clearly demonstrates that MS smoke acetaldehyde yields correlate significantly with two indicators of total MS smoke formation, i.e., with both "tar" and carbon monoxide yields. These results suggest that MS AA deliveries are affected more by cigarette design characteristics, e.g., ventilation and overall deliveries, than by specific tobacco blend components.

The superior correlations with carbon monoxide was attributed to the fact that acetaldehyde is primarily a gas phase constituent of MS smoke, as is carbon monoxide; "tar" is the sum of the particulate phase constituents, excluding nicotine and water.[7] Many studies have shown that carbon monoxide in MS smoke is formed by a number of different types of processes, each undoubtedly representing numerous reactions.[24] These include thermal decomposition as well as combustion of tobacco materials as well as oxidation of carbon and reduction of carbon dioxide. Similarly, it is likely that MS smoke acetaldehyde is formed via numerous reaction pathways, from various tobacco components. It has recently been suggested that tobacco-natural polysaccharides, e.g., cellulose, are major precursors of MS acetaldehyde.[6]

As described above in Case 2a, the relationship of the ratio MS acetaldehyde/"tar" vs. "tar" may reveal some additional insight into smoke chemistry. This relationship is plotted in Figures 6-7 for two representative years, 1985 and 1992, the same years used in Figures 3-4. Underlying summary data for this ratio is also listed in Table 3. The variation in the ratio at low "tar" values, as illustrated in Figures 6-7, is due, at least in part, to the relative variability of the analytical methods used to quantify MS acetaldehyde and "tar" (and MS CO) for very low delivery cigarettes. Nonetheless, visual examination of Figures 6-7 indicates that the ratio of MS smoke acetaldehyde/"tar" is essentially independent of the "tar" yield. This qualitative conclusion can be somewhat quantified by correlating the data using a linear model (eq. 3; see Table 10 for data summary). In all cases for the years studied, a near zero slope was obtained. In a few cases, the linear model is statistically significant, though the percent of the variation in the ratio is only weakly explained by "tar" yield. In the other cases, there is simply no

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relationship between the parameters. This data suggests that the ratio MS smoke acetaldehyde/"tar" is independent of the "tar" yield.

MS smoke acetaldehyde yield/"tar" = slope x ("tar") + intercept (3)

Similarly, the ratio MS acetaldehyde/carbon monoxide vs. carbon monoxide (eq. 4) is plotted in Figure 8 for 1985. A similar plot is obtained when using the data for 1993. See data summary in Table 8 and the correlation results in Table 10. Examination of these two relationships suggests that the ratio MS smoke acetaldehyde/CO cannot be predicted by the CO yield.

MS smoke acetaldehyde yield/"MS CO" = slope x ("MS CO") + intercept (4)

MS SMOKE ACETALDEHYDE YIELD AND REDUCING SUGARS IN TOBACCO

The hypothesis has been advanced that sugars added to the blends of commercial cigarettes increase the amount of acetaldehyde in MS smoke.[4,25] Both reducing sugars and non-reducing sugars are known tobacco additives.[6,26,27] Table 11 shows the structures of the reducing sugars sometimes used in some commercial cigarettes; note that sucrose is not a reducing sugar. Reducing sugars can be readily quantified as described in the Experimental Section.

Total reducing sugars was quantified for some of the cigarettes in the Philip Morris database for which MS smoke acetaldehyde data is available (1985-1988 and 1990-1993). A summary of the data is shown in Table 12. There is a modest decrease in reducing sugars from 8.1-8.7 % (on a dry weight basis) from the earlier years of this data set to ca. 6.4-7.1 (mean values of the data) in the 1989 to 1993 time period. This is graphically illustrated in Figure 9. The statistically significant differences in the mean values for the years for which data is available are also shown in Table 12.

No correlation was observed between MS smoke acetaldehyde yield or the MS smoke acetaldehyde/"tar" ratio with reducing sugars. Significant scatter is observed in these relationships, as indicated in Table 12. Figures 10-11 illustrate two representative data sets for the AA/"tar" vs. "tar" relationship, chosen to cover the higher end of the observed RS levels.

CONCLUSIONS

Previously unpublished data was used from the Philip Morris database of US commercial cigarettes, including cigarettes made by manufacturers other than Philip Morris. The data, correlations, and conclusions reported herein are consistent with the data from the published literature, including the recent outstanding 1999 Massachusetts Benchmark Study,[7] the less comprehensive 1997 Labstat Report for the Commonwealth of Massachusetts,[8] and other related studies.[9,28,29] The following conclusions are based on all three studies and are consistent with other literature results.

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1. MS smoke acetaldehyde is significantly correlated with "tar" yield and also with MS smoke carbon monoxide, using either a linear model (this work) or a quadratic model (Massachusetts Benchmark Study).

2. MS acetaldehyde yield is not correlated with reducing sugar concentration in tobacco blend in these series of commercial cigarettes.

3. Over the time period 1985-1993, for the available data, the concentration of reducing sugars decreased from ca. 8.1-8.7 to ca. 6.4-7.1 (mean value of the brands).

4. The correlations found between MS smoke acetaldehyde yield *and* "tar" and MS smoke carbon monoxide support the conclusion that both acetaldehyde and carbon monoxide yields for this wide range of US commercial cigarettes are affected more by cigarette design characteristics influencing total smoke production, such as filter ventilation, than by specific additives.

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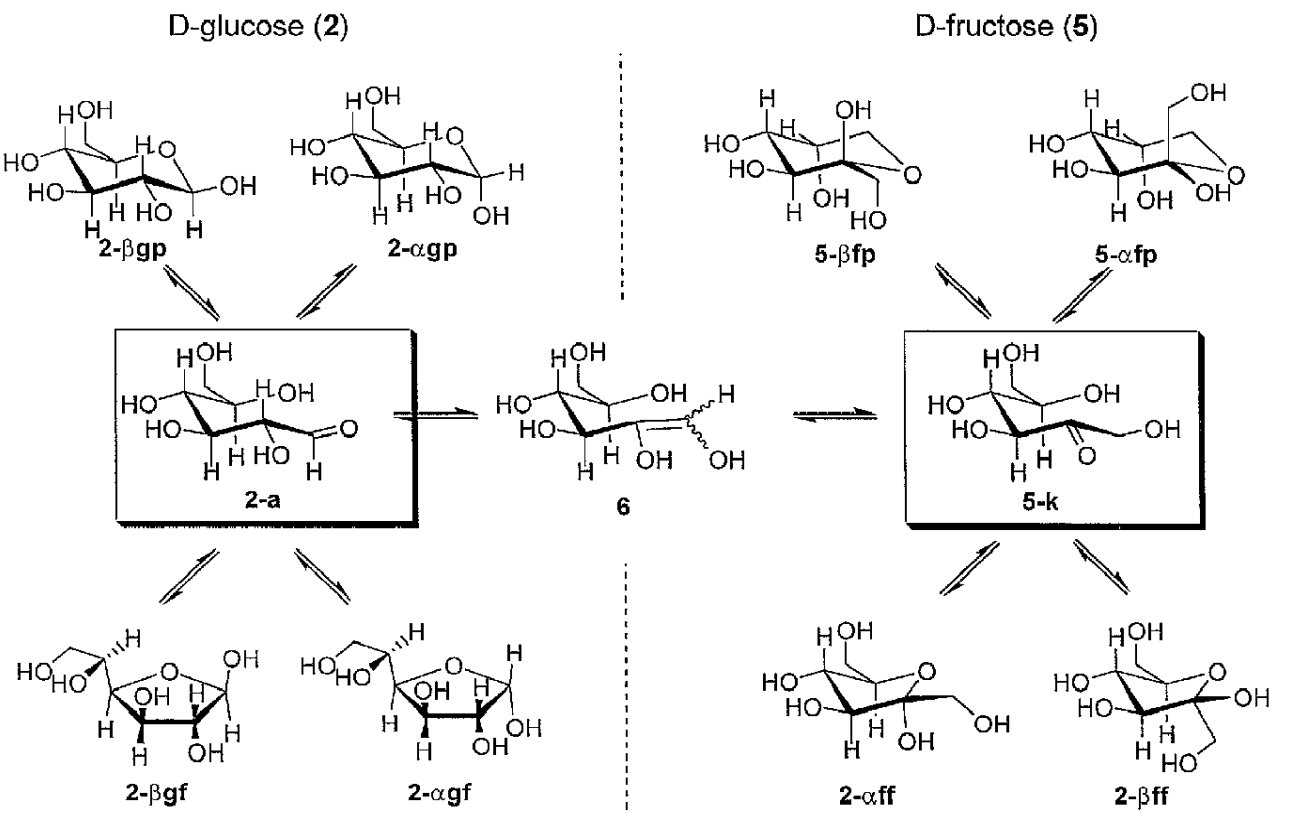

Figure 1. The isomerizations of D-glucose (**2**) and D-fructose (**5**) via the intermediacy of **2-a** and **5-k**, respectively, and the enediol **6**. The aldehyde hydrate [$RCH(OH)_2$] is not shown. The furanose forms of **2** and the pyranose forms of **5** are known to be minor contributors.

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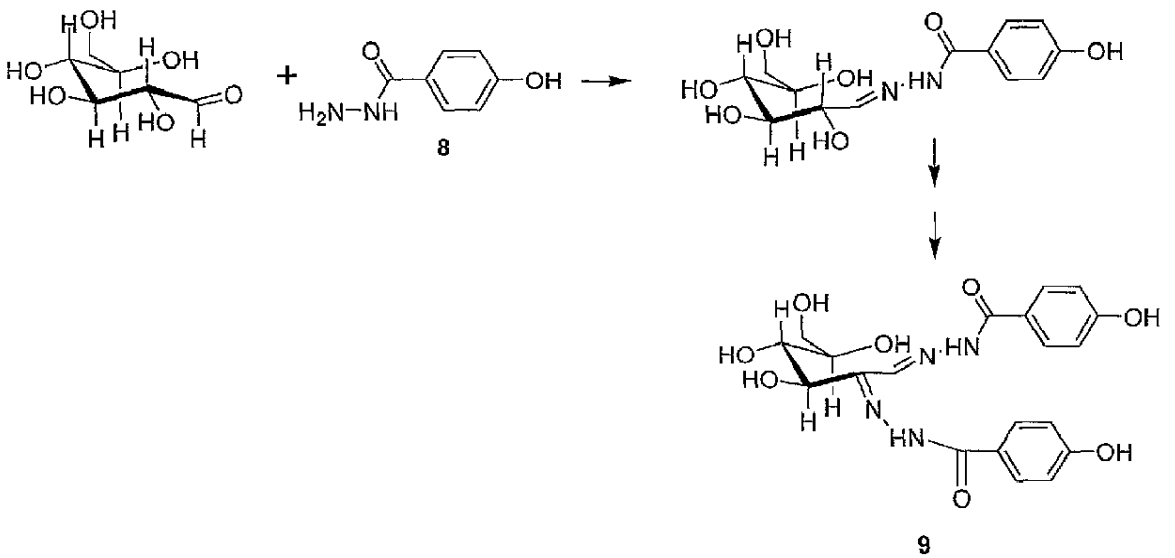

Figure 2. The reaction of the *aldehydo* form of D-glucose (see Figure 1) with 4-hydroxybenzoic acid hydrazide (**8**), a reagent used in the colorimetric analysis of reducing sugars. The osazone **9** has been proposed to be the final product.[10,19,20]

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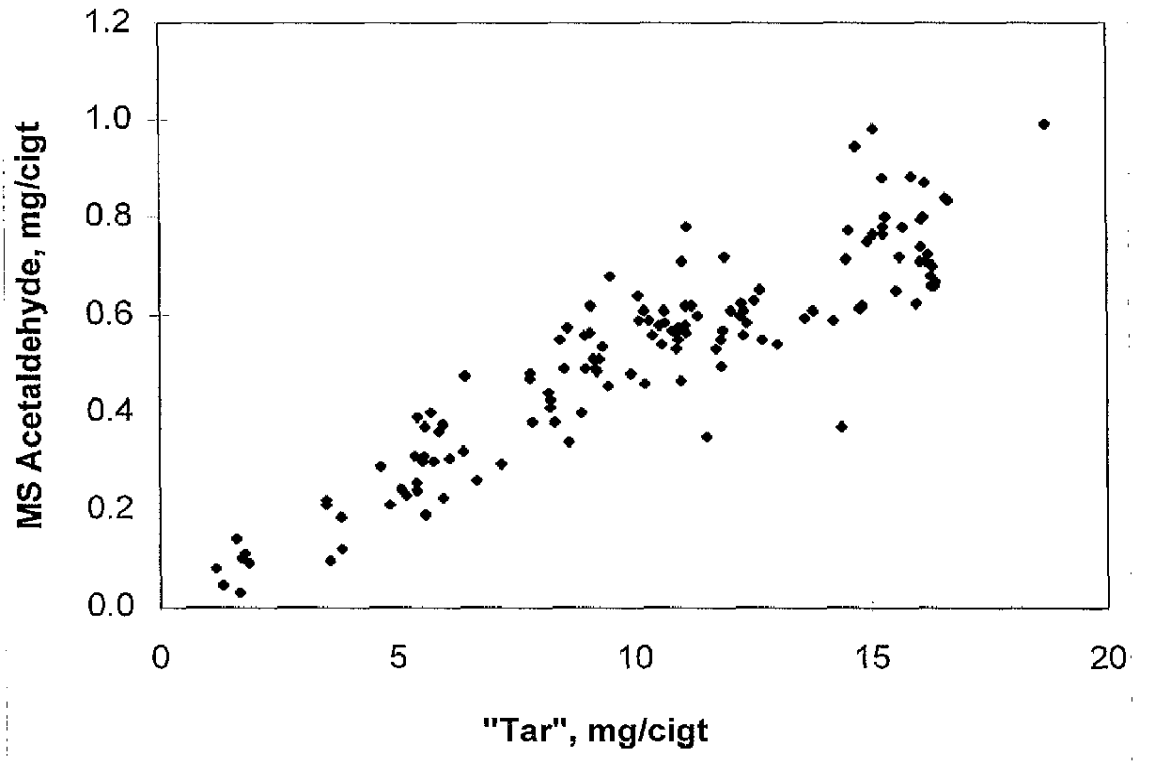

Figure 3. Plot of FTC MS smoke acetaldehyde vs. "tar" for 1985 (n = 135).

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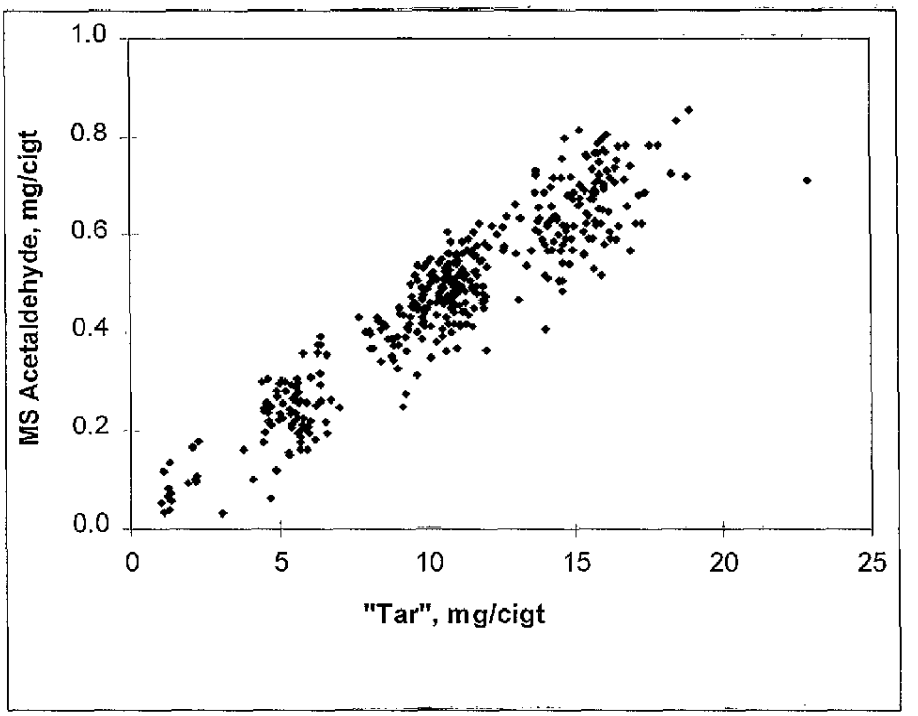

Figure 4. Plot of FTC MS smoke acetaldehyde vs. "tar" for 1992 (n = 422).

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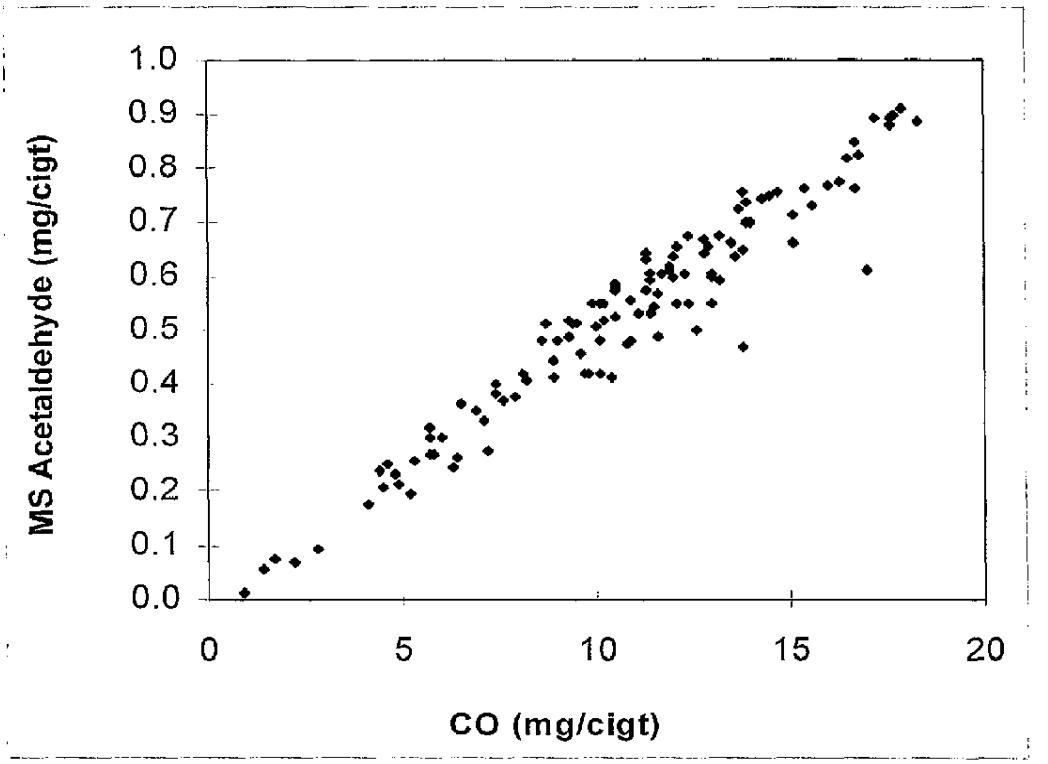

Figure 5. Plot of FTC MS smoke acetaldehyde vs. carbon monoxide for 1993 (n = 117).

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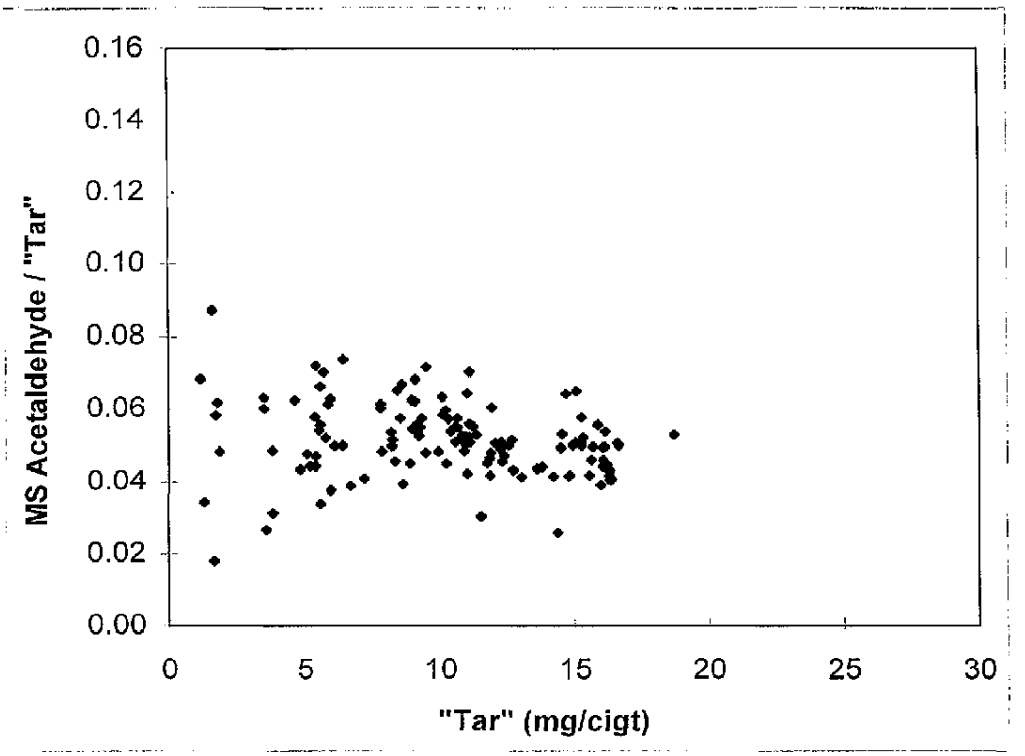

Figure 6. Plot of the ratio FTC MS acetaldehyde/"tar" vs. "tar" for 1985 (n = 135).

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Source: https://www.industrydocuments.ucsf.edu/docs/zjcl0001

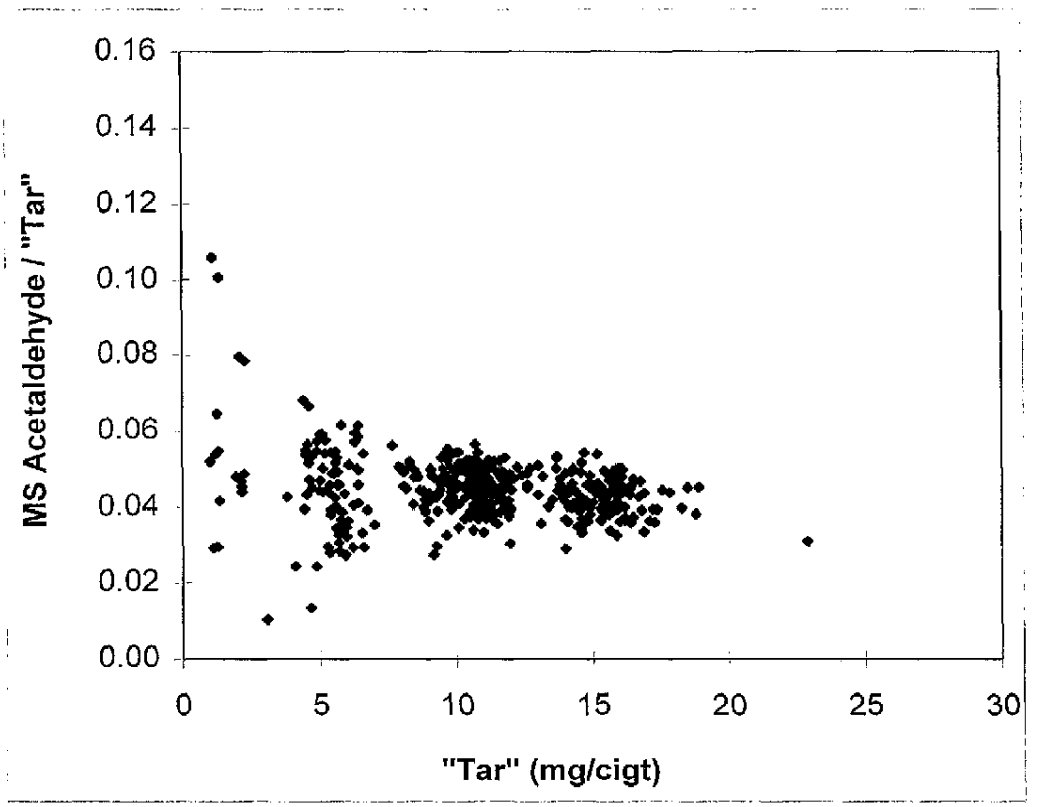

Figure 7. Plot of the ratio FTC MS acetaldehyde/"tar" vs. "tar" for 1992 (n = 422).

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Source: https://www.industrydocuments.ucsf.edu/docs/zjcl0001

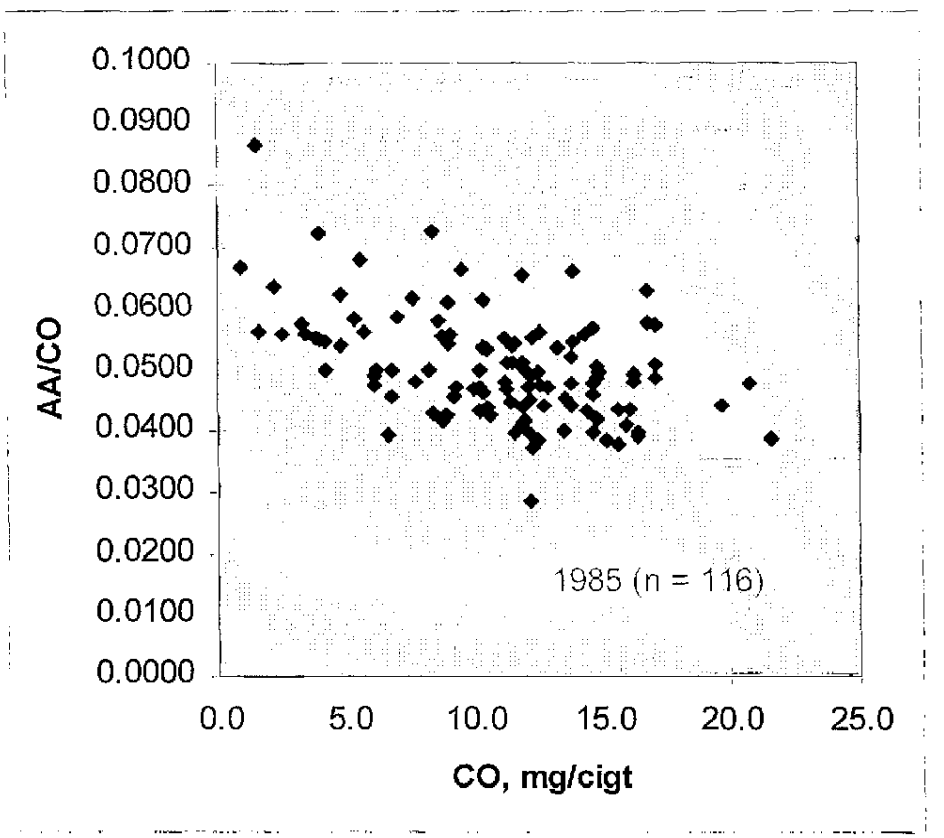

Figure 8. Plot of the ratio FTC MS smoke acetaldehyde/CO vs. CO for 1985 (n = 116).

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Source: https://www.industrydocuments.ucsf.edu/docs/zjcl0001

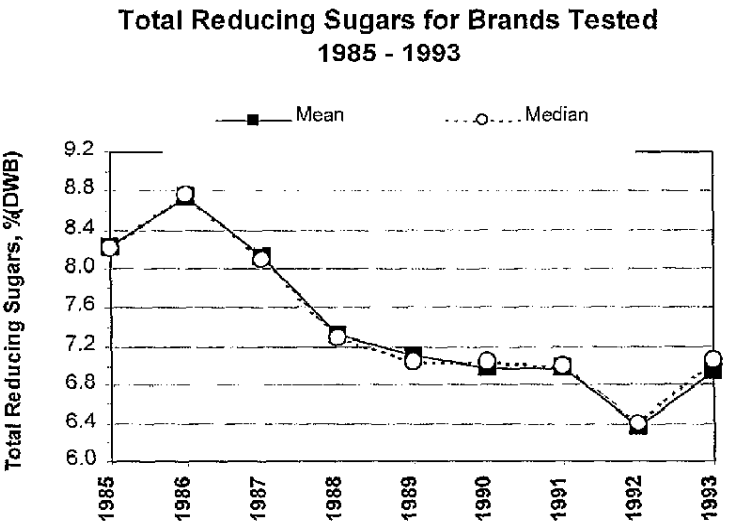

Figure 9. Plot of percent total reducing sugars (mean and median values, on a dry weight basis) for 1975 through 1993. For the number of samples and details of statistical significance, see Table 12.

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Source: https://www.industrydocuments.ucsf.edu/docs/zjcl0001

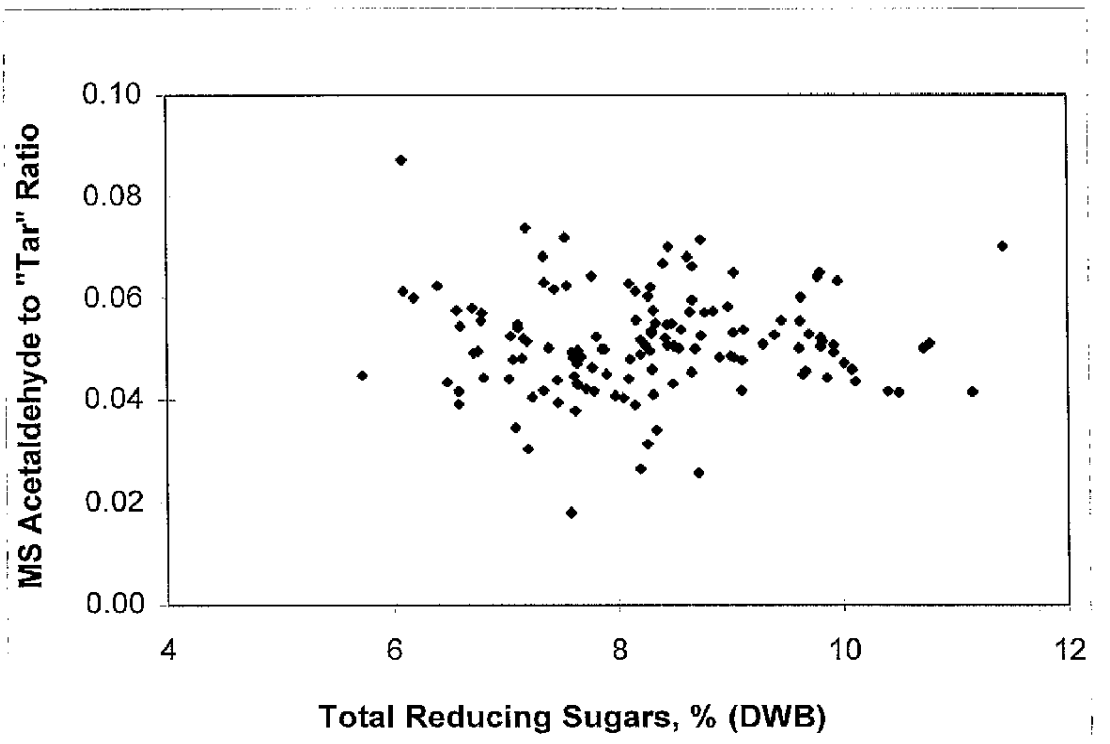

Figure 10. Plot of the ratio FTC MS smoke acetaldehyde/"tar" vs. total reducing sugars for 1985 (n = 135).

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Source: https://www.industrydocuments.ucsf.edu/docs/zjcl0001

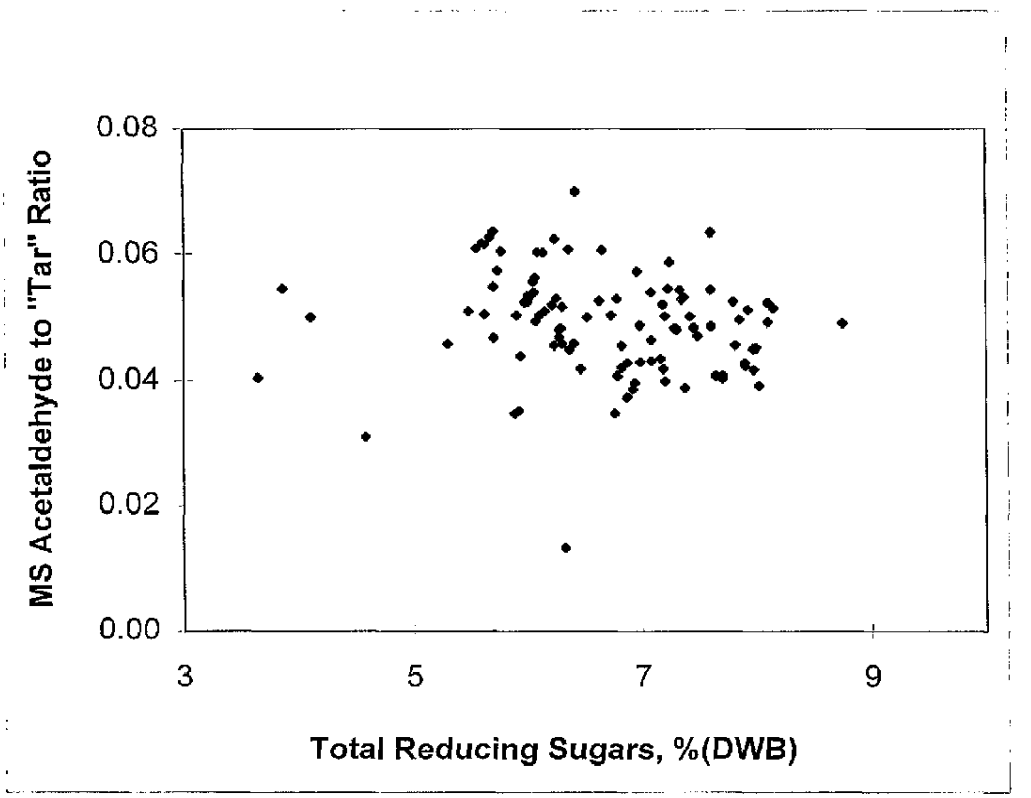

Figure 11. Plot of the ratio FTC MS smoke acetaldehyde/"tar" vs. total reducing sugars for 1993 (n = 102).

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Table 1. Puff profiles used in this work and in the literature.

	Puff volume (mL)	Puff duration (sec)	Interval between puffs (sec)	Ventilation hole blocking (%)
FTC[a]	35	2	58	0
Labstat Jan. 30, 1997 Report[b] **for Massachusetts – "Average"**	45	2	34	50
Labstat Jan. 30, 1997 Report[b] **for Massachusetts – "Intense" (or "Heavy")**	60	2	26	100
1999 Massachusetts Benchmark Study[c,d]	45	2	28	50

[a] 'Federal Register', Vol. 32, Number 147, August 1, 1967. See also 'Federal Register', Vol. 45, Number 134, July 10, 1980. [b] From Reference 8. [c] From Reference 7. [d] As stated in the Report: "All were taped to achieve 50 % ventilation hole blocking, conditioned under 72 °F +/- 2 and 60 +/- 2 % relative humidity and puffed under the Massachusetts puffing regime of 45 +/- 0.5 mL puff volume with 2 +/- 0.1 second puff duration once every 30 +/- seconds according to the 1999 Massachusetts Benchmark Study Protocol."

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Table 2. Comparison of MS smoke characteristics of nicotine and acetaldehyde.

Smoke Property	Nicotine	Acetaldehyde
Mainstream smoke phase	>99% particulate phase	>95% gas phase
Tobacco → mainstream smoke precursor	Thermal decomposition of nicotine salts of natural tobacco carboxylic acids	Formed from many precursors, primarily from tobacco cellulose, other polysaccharides
Formation mechanism	Evaporative transfer from nicotine in tobacco	Pyrolysis and combustion product
Stability in smoke and during analysis	Stable	Likely to react with ammonia, amino acids, other amines. Can polymerize. Can form hydrate with water.

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Table 3. Values of MS smoke "tar" and MS acetaldehyde and the ratio of MS acetaldehyde/"tar" of US commercial cigarettes using the FTC method. Data from the Philip Morris USA Testing Laboratory.

	"Tar" (mg/cigarette)			MS Acetaldehyde (mg/cigarette)			MS Acetaldehyde/"tar"		
Year	**n[a]**	**Mean +/- standard deviation**	**Range**	**n**	**Mean +/- standard deviation**	**Range**	**n**	**Mean +/- standard deviation**	**Range**
1985	196	10.6 ± 4.7	1.1-28.3	135	0.52 ± 0.21	0.03–0.99	135	0.051 ± 0.010	0.018–0.087
1986	237	11.2 ± 4.9	1.1-28.4	142	0.51 ± 0.20	0.02-0.93	142	0.050 ± 0.010	0.014-0.083
1987	235	10.5 ± 4.4	1.1-28.4	185	0.53 ± 0.21	0.02-0.93	185	0.054 ± 0.011	0.011-0.099
1988	233	10.8 ± 4.2	1.2-24.2	179	0.56 ± 0.20	0.07-0.97	179	0.056 ± 0.009	0.028-0.091
1989	265	10.9 ± 4.1	1.2-23.5	4	[b]	[b]	4	[b]	[b]
1990	293	11.0 ± 4.2	1.3-22.9	116	0.59 ± 0.24	0.08-1.07	116	0.057 ± 0.012	0.029-0.090
1991	347	11.0 ± 4.3	1.0-24.7	325	0.45 ± 0.18	0.01-0.85	325	0.041 ± 0.008	0.008-0.071
1992	492	10.8 ± 4.1	1.0-24.6	422	0.47 ± 0.18	0.03-0.85	422	0.045 ± 0.008	0.010-0.106
1993	362	10.7 ± 4.2	0.5-22.6	102	0.54 ± 0.20	0.01-0.91	102	0.049 ± 0.008	0.013-0.070

[a] "n" is the number of brands. [b] Not calculated due to the small number of brands tested for MS smoke acetaldehyde in 1989.

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Table 4. Mean values of MS smoke acetaldehyde and "tar" from US commercial cigarettes. Data from literature reports.

Source of data		Puff profile	"Tar" (mg/cigarette)			Acetaldehyde (mg/cigarette)	
	Ref.		Number of brands	Mean +/- standard deviation	Range	Mean +/- standard deviation	Range
Labstat, 1997	8	FTC	8	8.6 ± 5.0	0.5-16	0.385 ± 0.226	0.003-0.705
Massachusettes Benchmark Study (1999)	7	FTC	26	10.54 ± 6.94	0.49-26.7	n/d[a]	n/d[a]
Massachusettes Benchmark Study (1999)	7	MBS	26	23.64 ± 10.90	6.08-48.73	1.458 ± 0.453	0.596 – 2.133
Chepiga, et al. (2000)	9	FTC	8[b]	3.3 ± 0.90	0.7-7.2	0.237 ± 0.047	0.0961-0.389
Chepiga, et al. (2000)	9	FTC	11[c]	9.9 ± 0.40	8.10-11.6	0.649 ± 0.045	0.342-0.812
Chepiga, et al. (2000)	9	FTC	10[d]	15.4 ± 0.4	12.9-17.2	0.916 ± 0.028	0.726-1.071

[a] Not determined. [b] Eight brands were selected from an arbitrary "ultra low tar" range. [c] Eleven brands were selected from an arbitrary "full flavor low tar" range. [d] Ten brands were selected from an arbitrary "full flavor tar" range.

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Table 5. For data from the Philip Morris database (see Table 3), smoking parameters and regression analysis data for the linear model of MS smoke acetaldehyde vs. "tar"; i.e., using the linear relationship model:

"MS smoke acetaldehyde yield" = slope x ("tar") + intercept

Sample Description		Best fit parameters			
Year	**Number of brands**	**Slope**	**Intercept**	**r^2**	**p**
1985	135	0.0451	0.0545	0.832	<0.00001
1986	142	0.0436	0.0615	0.794	<0.00001
1987	185	0.0446	0.0757	0.843	<0.00001
1988	179	0.0448	0.0962	0.836	<0.00001
1989	4	[a]	[a]	[a]	[a]
1990	116	0.0512	0.0531	0.826	<0.00001
1991	325	0.0378	0.0311	0.855	<0.00001
1992	422	0.0409	0.0344	0.870	<0.00001
1993	102	0.0460	0.0329	0.842	<0.00001

[a] Not determined due to small sample size.

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Table 6. Smoking parameters and regression analysis data for MS smoke acetaldehyde vs. different smoke parameters ("tar" and MS CO) using equation 2. Correlations are from literature reports (see Table 4).[a]

$$\text{MS smoke acetaldehyde yield} = \underline{a}\ (\text{"MS CO"})^2 + \underline{b}\ (\text{"MS CO"}) + \underline{c} \qquad (2)$$

		Best fit parameters for correlation with MS smoke acetaldehyde with either "tar" or MS carbon monoxide						
Sample Description				Coefficients of best fit curve (using equation 2)				
Source of data	Number of brands	MS smoke parameter	Puff profile	a	b	c	r^2	p
Massachusettes Benchmark Study[b]	26	"tar"	MBS	-1.2808	94.978	79.124	0.8209	n/r
Massachusettes Benchmark Study[b]	26	MS CO	MBS	-2.2875	163.83	-930.76	0.9257	n/r
Chepiga, et al.[c]	25	"tar"	FTC	0[d]	n/r[e]	n/r	0.91	n/r

[a] Data expressed in mg/cigarette for all parameters. [b] Data from reference 7. [c] Data from reference 9. [d] In the Chepiga, et al.[9] study, the authors used a linear regression model, i.e., a = 0. [e] Not reported.

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Table 7. Correlation coefficients for linear relationships between various MS smoke constituents, using Labstat data for the Commonwealth of Massachusetts.[a] The different puff profiles are described in Table 1.[b]

	acetaldehyde (FTC)	**"tar" (FTC)**	**"tar" (average)**	**"tar" (intense)**	**CO (FTC)**	**CO (average)**
acetaldehyde (FTC)	1					
"tar" (FTC)	(0.962)	1				
"tar" (average)	0.988 (0.975)	(0.964)	1			
"tar" (intense)	0.969 (0.932)	(0.948)	0.991 (0.984)	1		
CO (FTC)	(0.968)	(0.947)	(0.967)	(0.968)	1	
CO (average)	0.947 (0.936)	(0.878)	0.963 (0.963)	0.965 (0.958)	(0.933)	1
CO Intense	0.862 (0.771)	(0.804)	0.899 (0.862)	0.925 (0.913)	(0.853)	0.950 (0.910)

[a] Data from reference 8. [b] Data expressed in mg/cigarette for all parameters. Numbers in ( ) using eight brands. All others using ten brands.

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Table 8. Values of MS smoke carbon monoxide and acetaldehyde in the MS smoke of US commercial cigarettes using the FTC method. Data are from the Philip Morris USA Testing Laboratory.

	MS carbon monoxide (mg/cigarette)			Acetaldehyde (mg/cigarette)		Acetaldehyde/MS carbon monoxide	
Year	**n[a]**	**Mean +/- standard deviation**	**Range**	**Mean +/- standard deviation**	**Range**	**Mean +/- standard deviation**	**Range**
1985	116	10.8 ± 4.3	0.9-21.6	0.53 ± 0.21	0.06–1.06	0.051 ± 0.009	0.029-0.087
1993	117	10.8 ± 4.0	0.90-18.3	0.53 ± 0.20	0.01-0.91	0.048 ± 0.006	0.014-0.059

[a] "n" is the number of brands.

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Table 9. For data from the Philip Morris database (see Table 8), smoking parameters and regression analysis data for the linear model of MS smoke acetaldehyde vs. MS carbon monoxide; i.e., using the linear relationship model:

"MS smoke acetaldehyde yield" = slope x (MS carbon monoxide) + intercept

Sample Description		Best fit parameters			
Year	**Number of brands**	**Slope**	**Intercept**	**r^2**	**p**
1985	116	0.0435	0.0590	0.833	<0.00001
1993	117	0.0491	-0.0015	0.934	<0.00001

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Table 10. For data from the Philip Morris database (see Tables 3 and 8), smoking parameters and regression analysis data for the linear model of MS smoke acetaldehyde/"tar" vs. "tar" and MS smoke acetaldehyde/MS CO vs. MS CO using the linear relationship models.

Sample Description		Best fit parameters			
Year	**Number of brands**	**Slope ± Standard Deviation**	**Intercept**	**r^2**	**p**
MS smoke acetaldehyde yield/"tar" = slope x ("tar") + intercept					
1985	135	-0.0005±0.0002	0.0562	0.0425	0.0165
1986	142	-0.0002±0.0002	0.0523	0.0093	0.2526
1987	185	-0.0009±0.0002	0.0626	0.115	<0.00001
1988	179	-0.0010±0.0002	0.0664	0.195	<0.00001
1989	4	[a]	[a]	[a]	[a]
1990	116	-0.0006±0.0002	0.0642	0.060	0.0083
1991	325	0.0001±0.0001	0.0395	0.0027	0.347
1992	422	-0.0005±0.0002	0.0562	0.0425	0.0165
1993	102	-0.0013±0.0009	0.0575	0.0209	0.147
MS smoke acetaldehyde yield/"MS CO" = slope x ("CO") + intercept					
1985	116	-0.0010±0.0002	0.061	0.221	<0.00001
1993	117	-0.0004±0.0001	0.044	0.070	0.0039

[a] Not determined due to small sample size.

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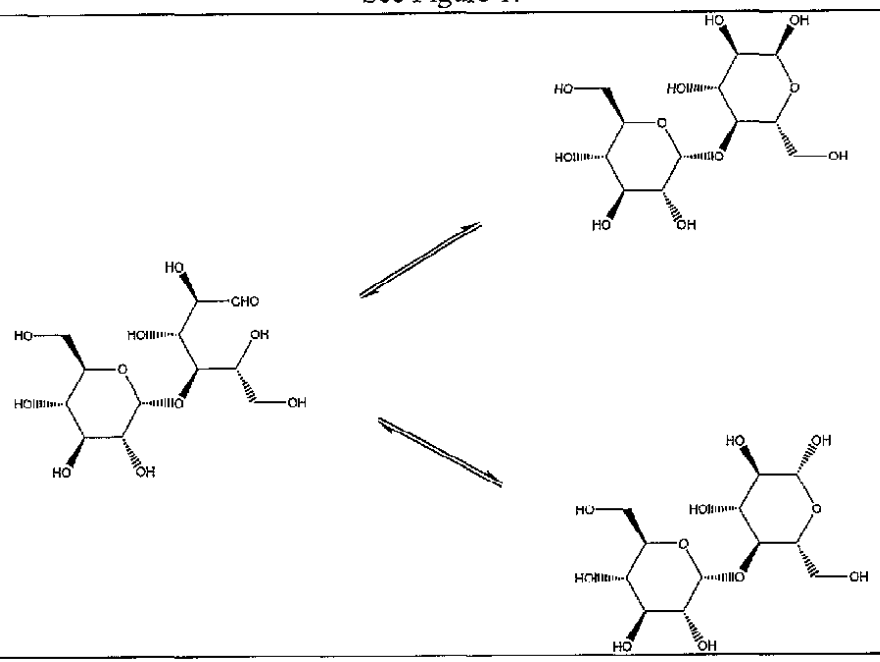
Table 11. Reducing sugars, or mixtures containing reducing sugars, sometimes used as additives to tobacco blends.[a]

Substance	Structure[b, c]
D-Glucose (**2**) Corn sugar Corn syrup Dextrose	See Figure 1.
D-Fructose (**5**)	See Figure 1.
Maltose (**10**)	

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Source: https://www.industrydocuments.ucsf.edu/docs/zjcl0001

Invert sugar (Obtained by hydrolysis of sucrose.)	A mixture of ca. 50% D-glucose and 50% D-fructose
Honey	Contains 70-80% D-glucose and D-fructose; 2-10% sucrose
Carob bean	Contains 30-70% (usually 40-50%) sucrose, D-fructose, maltose and D-glucose, among others
Licorice	Contains 3-4% sugars (D-glucose and sucrose)
Invert sugar (Obtained by hydrolysis of sucrose.)	A mixture of ca. 50% D-glucose and 50% D-fructose
Honey	Contains 70-80% D-glucose and D-fructose; 2-10% sucrose (a non-reducing sugar)[d]
Carob bean	Contains usually ca. 40-50% sucrose, D-fructose, maltose and D-glucose, among others[d]
Licorice	Contains a 3-4% mixture of D-glucose and sucrose[d]

[a] Sucrose, also added as casings in cigarette manufacture, is not a reducing sugars and was not quantified in the analyses used herein. [b] In some cases, multiple isomers can represent the substance. The actual composition in the tobacco matrix will depend on various matrix conditions, e.g., water concentration, relative concentration of acids and bases and other substances, and temperature. [c] Not all structural isomers illustrated. [d] Data from: Leung, A. Y.; Foster, S. *Encyclopedia of Common Natural Ingredients*; John Wiley: New York, 1996.

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Table 12. Total reducing sugars in blends of commercial cigarettes and correlations with MS smoke acetaldehyde and the ratio acetaldehyde/"tar".

Year	Reducing sugars (% in tobacco)[a]				Regression statistics		
					Number of brands	Correlation (r^2) of reducing sugars with:	
	Number of brands	Range	Mean +/- standard deviation	Statistical grouping		Acetaldehyde	Acetaldehyde/ "tar"
1985	162	5.3–11.4	8.2 ± 1.2	B	135	0.0899	0.0000
1986	187	5.7-12.1	8.7 ± 1.0	A	142	0.0715	0.0000
1987	193	5.9-11.4	8.1 ± 0.9	B	185	0.0872	0.0004
1988	182	5.7-9.2	7.3 ± 0.7	C	176	0.2349	0.0074
1989	210	4.9-10.0	7.1 ± 0.9	D	4	[c]	[c]
1990	236	4.6-9.4	7.0 ± 0.9	D	116	0.1633	0.0206
1991	281	4.7-9.2	7.0 ± 0.8	D	264	0.1387	0.0004
1992	420	4.0-9.4	6.4 ± 0.8	E	420	0.0847	0.0541
1993	243	3.6-9.4	6.9 ± 1.0	D	102	0.0436	0.0209

[a] Total reducing sugars are not corrected to dry weight basis. [b] Means with the same letter are not significantly different at $\alpha = 0.05$. [c] Not determined due to small size of sample.

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